Fig. 7D shows detection of CTNNB1/PLAG1 transcripts using a probe with specificity for the 3' UTR of PLAG1 (probe KK64);

Fig. 8 shows the sequence of the PLAG2 cDNA with the open reading frame underlined;

Fig. 9 shows the nucleotide sequence of cDNA of CTNNB1 (β-catenin); and

Fig. 10 shows STSs used to generate the 300 kb cosmid contig mapping at chromosome 8q12 and encompassing PLAG1.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS--.

IN THE CLAIMS:

Please cancel original claims 1-25 and insert new claims 26-48 as follows:

--26. A nucleic acid in isolated form, comprising one of an oligonucleotide, a polynucleotide and a gene having a nucleotide sequence of at least a part of a T-gene selected from the group consisting of the PLAG subfamily of zinc finger protein genes, the CNNB1 gene and fusions thereof, or complementary or degenerate versions of the nucleotide sequence.

27. The nucleic acid as claimed in claim 26, wherein the nucleic acid is one of an oligonucleotide, a polynucleotide and a gene having a sequence of at least a part of a gene selected from the group consisting of PLAG1, PLAG2 and CNNB1, sequences complementary thereto and degenerate sequences thereof.

28. The nucleic acid as claimed in claim ~~26~~ 47, having homology with the zinc finger domains of the PLAG1 (pleomorphic adenoma gene 1) gene the nucleotide sequence of which is depicted in figure 4A, or ~~the~~ a complementary strand thereof, including modified, degenerate or elongated versions of both strands.

29. The nucleic acid as claimed in claim ~~26~~ 47, comprising the nucleotide sequence of the PLAG1 gene as depicted in figure 4A, or ~~the~~ a complementary strand thereof, including modified, degenerate or elongated versions of both strands.

30. The nucleic acid as claimed in claim 26, comprising the nucleotide sequence of the PLAG2 gene as depicted in figure 8A, or the complementary strand thereof, including modified, degenerate or elongated versions of both strands.

31. The nucleic acid as claimed in claim 26, comprising the nucleotide sequence of the CTNNB1 gene as depicted in figure 9, or the complementary strand thereof, including modified or elongated versions of both strands.

32. The nucleic acid as claimed in claim ~~26~~ 47, wherein the nucleic acid is labeled.

33. A macromolecule comprising a derivative of a nucleic acid in isolated form, comprising one of an oligonucleotide, a polynucleotide and a gene having a nucleotide sequence of at least a part of a T-gene selected from the group consisting of the PLAG (pleomorphic adenoma gene 1) subfamily of zinc finger protein genes, the ~~CNNB1~~ CTNNB1 (β-catenin) gene

and fusions thereof, or complementary or degenerate versions of the nucleotide sequence.

34. The macromolecule as claimed in claim 33, wherein the derivative is selected from the group consisting of:

a) a transcript corresponding to the nucleic acid;

b) cDNA corresponding to the nucleic acid;

c) sense or antisense DNA corresponding to the nucleic acid;

d) a nucleic acid including a gene, or a derivative thereof, isolated by using at least a part of a T-gene as one of a probe or primer;

e) a protein encoded by the nucleic acid; and

f) antibodies, or derivatives thereof, directed to the nucleic acid, the transcript, the cDNA and the protein.

35. The macromolecule as claimed in claim 34, wherein the derivative is labeled.

36. A diagnostic kit comprising one of a labeled nucleic acid as claimed in claim 26 and a labeled macromolecule derivative of the nucleic acid and one or more diagnostic reagents.

37. The kit as claimed in claim 36, wherein the kit comprises labeled T-gene specific and tail specific PLR primers.

38. The kit as claimed in claim 36, wherein the macromolecule is a set of labeled nucleic acid probes and the kit further comprises a restriction enzyme.

39. The kit as claimed in claim 36, wherein the macromolecule is a labeled probe for <u>in situ</u> diagnostics.

A3 cont

40. An <u>in situ</u> diagnostic method for diagnosing interphase and/or metaphase cells having a non-physiological proliferative capacity, comprising the steps:

a) designing a set of nucleotide probes based on a nucleic acid as claimed in claim 26, wherein at least one of the probes is hybridisable to a region of the aberrant gene substantially mapping at the same locus as a corresponding region of the wildtype gene and/or the same or another probe is hybridisable to a region of the aberrant gene mapping at a different locus than a corresponding region of the wildtype gene;

b) incubating one or more interphase or metaphase chromosomes or interphase or metaphase cells having a non-physiological proliferative capacity, with the probe(s) under hybridising conditions; and

c) visualising the hybridisation between the probe(s) and the gene.

41. A method of diagnosing cells having a non-physiological proliferative capacity, comprising the steps of:

a) taking a biopsy of a tumor to obtain cells to be diagnosed;

b) isolating a suitable T-gene-related macromolecule therefrom;

c) analysing the macromolecule thus obtained by comparison with a wildtype reference molecule.

Q3 cont

42. The method as claimed in claim 41, comprising the steps of:

a) taking a biopsy of a tumor to obtain cells to be diagnosed;

b) extracting total RNA thereof;

c) preparing at least one first strand cDNA of the mRNA species in the total RNA extract, which cDNA comprises a suitable tail;

d) performing one of a PCR and a RT-PCR using one of a PLAG gene specific primer, a tail-specific and a partner-specific/nested primer to amplify PLAG gene specific cDNA's;

e) separating the PCR products on a gel to obtain a pattern of bands;

f) evaluating the presence of aberrant bands by comparison to wildtype bands.

43. The method as claimed in claim 41, comprising the steps of:

a) taking a biopsy of a tumor to obtain cells to be diagnosed;

b) isolating total protein therefrom;

c) separating the total protein on a gel to obtain essentially individual bands;

d) hybridising the bands thus obtained with antibodies directed against a part of the protein encoded by a remaining part of the T-gene and against a part of the protein encoded by a substitution part of the T-gene;

A3 cont

e) visualising the antigen-antibody reactions and establishing the presence of aberrant bands by comparison with bands from wildtype proteins.

44. The method as claimed in claim 41, comprising at least some of the following steps:

a) taking a biopsy of a tumor to obtain cells to be diagnosed;

b) isolating total DNA therefrom;

c) digesting the DNA with a restriction enzyme;

d) separating the digest thus prepared on a gel to obtain a separation pattern;

e) hybridising the separation pattern in the gel or on the blot with a labeled nucleic acid in isolated form, comprising one of an oligonucleotide, a polynucleotide and a gene having a nucleotide sequence of at least a part of a T-gene selected from the group consisting of the PLAG subfamily of zinc finger protein genes, the CNNB1 gene and fusions thereof, or complementary or degenerate versions of the nucleotide sequence; and

f) visualising the hybridisations and establishing the presence of aberrant bands by comparison to wildtype bands.

45. A method for identifying a T-gene comprising the steps of:

a) preparing one of a probe and a primer of a nucleic acid as claimed in claim 26;

b) isolating a gene which hybridises to the probe or primer.

A3 cont

46. A method for inhibiting expression of a T-gene comprising contacting a cell with a derivative as claimed in claim 33, wherein the derivative is one of an antisense nucleic acid, a nucleic acid coding for an antisense molecule, or otherwise interferes with expression of a T-gene, and an antibody or a derivative thereof.--

IN THE ABSTRACT:

A4

After the claims, please insert a page containing the Abstract Of The Disclosure, which is attached hereto as a separately typed page.

REMARKS

Amendments have been made to the specification to place the application in conformance with standard United States Patent practice.

Original claims 1-25 have been cancelled by this Preliminary Amendment. These claims have been rewritten as claims 26-46 in order to eliminate the multiple dependencies and to conform the claims to customary United States Patent practice. No new matter is added by the above-referenced amendments.